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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 10/672,626 | 09/26/2003 | Amy F.T. Arnsten | Y03-077 | 8080 |

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| EXAMINER | |
|---|---|
| CLAYTOR, DEIRDRE RENEE | |
| **ART UNIT** | **PAPER NUMBER** |
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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/672,626 | ARNSTEN ET AL. | |
| | Examiner | Art Unit | |
| | Renee Claytor | 1617 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *4/17/2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-4,10,12,14 and 18-21* is/are pending in the application.

4a) Of the above claim(s) *5-9,11 and 13* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,10,12,14 and 18-21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on *26 September 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *3/7/2005, 10/11/2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

Applicant's election without traverse of Group I in the reply filed on 4/17/2007 is acknowledged. Applicant's election of the species of CNS disorder as bipolar disorder is further acknowledged. Claims 1-4, 10, 12, 14, and 18-21 are being examined on their merits herein.

### *Claim Objections*

Claims 18-20 objected to because of the following informalities: The claims are dependent on a canceled claim. Appropriate correction is required.

### *Claim Rejections – 35 USC § 112*

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-3, 10, 12, 14 and 18-21 rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for certain types of CNS disorder, including bipolar disorder with chelerythrine, does not reasonably provide enablement for all CNS disorders with all compounds of formula (I) or (II). The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The instant specification fails to provide information that would allow the skilled artisan to practice the instant invention without undue experimentation. Attention is

directed to *In re Wands*, 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors: (1) the nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

**(1) The Nature of the Invention**: The rejected claims 1-3, 10, 12, 14 and 18-21 are drawn to a method for treating a CNS disorder or impaired cognitive performance in a subject comprising administration an effective amount of a compound of formula (I) or (II).

**(2) The state of the prior art:** The state of the art regarding treatment of various types of CNS disorders and impaired cognitive performance is high. However the state of the art regarding treatment for all CNS disorders and impaired cognitive performance with all compounds according to formulas (I) or (II) is underdeveloped. The skilled artisan would view that the treatment of all types of CNS disorders and impaired cognitive performance with all compounds of formulas (I) or (II) is highly unlikely.

**(3) The relative skill of those in the art:** The relative skill of those in the art is high.

**(4) The breadth of the claims:** Claims 1-3, 10, 12, 14 and 18-21 embrace a method for treating a CNS disorder or impaired cognitive performance in a subject comprising administration of an effective amount of a compound of formula (I) or (II).

**(5) The amount of guidance or direction presented:** In the instant case, working examples are presented for treating manic episodes and learning and memory tasks with chelerythrine in the specification on pages 19-23, in which chelerythrine was shown to increase performance on learning and memory tasks as well as improve the stress response (involving manic episodes). However, there are a lack of working examples presented in the specification as filed showing how to treat all CNS disorders with all compounds of formulas (I) and (II). For example, the compounds of formulas (I) and (II) have many possible substitutions that can be applied to $R^1$, $R^2$, $R^3$, $R^4$, $R^5$, $R^6$, $R^7$, $R^8$, $R^9$, and $R^{10}$ thereby leading to distinct chemical compounds. Because each compound is distinct structurally, each compound may have different reactivity, solubility, oral bioavailability etc. Note that lack of a working example is a critical factor to be considered, especially in a case involving an unpredictable and undeveloped art. See MPEP § 2164.

**(6) The presence or absence of working examples:** Applicant provides working examples for treating learning and memory disorders and bipolar disorders with chelerythrine. However, Applicant does not provide any working examples for treating all CNS disorders with all compounds for formulas (I) and (II).

**(7) The quantitation of experimentation necessary:** Claims 1-3, 10, 12, 14 and 18-21 read on a method for treating a CNS disorder or impaired cognitive

performance comprising administration of a compound of formulas (I) or (II). As discussed above, the specification provides examples for treating learning and memory disorders and bipolar disorders with chelerythrine but the specification fails to provide support for treating all CNS disorders and impaired cognitive performance. As discussed above, compounds of formulas (I) and (II) have distinct structures, lending to different reactivity, solubility and oral bioavailability etc. Applicant fails to provide information sufficient to practice the claimed invention, absent undue experimentation. Genetech, 108 F.3d at 1366 states that "a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion" and "patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable".

Claim 20 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treating learning and memory tasks and mania by administration of chelerythrine, does not reasonably provide enablement for protecting a subject from developing a CNS disorder by administering chelerythrine (Examiner interprets the claim as "prevention" of the development of a CNS disorder). The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The instant specification fails to provide information that would allow the skilled artisan to practice the instant invention without undue experimentation. Attention is

directed to *In re Wands*, 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors: (1) the nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

**(1) The nature of the invention**: The rejected claim 20 is drawn to a method comprising protecting a subject from developing a CNS disorder by administering a pharmaceutical composition.

**(2) The state of the prior art**: The state of the art regarding treating various types of CNS disorders and impaired cognitive performance is high. However, the state of the art regarding prevention of CNS disorders is underdeveloped.

**(3) The relative skill of those in the art**: The relative skill of those in the art is high.

**(4) The breadth of the claims**: Claim 20 embraces a method comprising protecting a subject from developing a CNS disorder by administering to a subject a pharmaceutical composition.

**(5) The amount of guidance or direction presented:** In the instant case, working examples are presented for treating manic episodes and learning and memory tasks with chelerythrine in the specification on pages 19-23 in which chelerythrine was

shown to increase performance on learning and memory tasks as well as improve the stress response (involving manic episodes). However, there are a lack of working examples presented in the specification as filed showing how to prevent CNS disorders. Note that lack of a working example is a critical factor to be considered, especially in a case involving an unpredictable and undeveloped art. See MPEP § 2164.

**(6) The presence or absence of working examples:** Applicant does not provide any working examples for the prevention of CNS disorders.

**(7) The quantitation of experimentation necessary:** Claim 20 reads on a method comprising protecting a subject from developing a CNS disorder by administration of a pharmaceutical composition. As discussed above, the specification provides examples for treating learning and memory disorders and bipolar disorders but the specification fails to provide support for the prevention of CNS disorder. Applicant fails to provide information sufficient to practice the claimed invention, absent undue experimentation. Genetech, 108 F.3d at 1366 states that "a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion" and "patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable".

***Claim Rejections – 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-4, 10, 18-21 rejected under 35 U.S.C. 103(a) as being unpatentable over Aylward et al. (PG-Pub 2003/0195168) in view of Herbert et al. (Biochemical and Biophysical Research Communications (1990) 172 (3), pgs. 993-999).

Aylward et al. teaches that it is known in the art to treat PKC-related conditions with agents known to lower higher than normal PKC levels and that a PKC mediated disorder includes bipolar disorder (paragraphs 0041 and 0042). Because it is taught that antagonists of PKC treat bipolar disorder, it is obvious to treat bipolar disorder regardless of how it is induced.

Aylward et al. does not teach that chelerythrine treats bipolar disorder.

Herbert et al. teach that chelerythrine is a potent, selective antagonist of the PKC (see abstract and results).

Accordingly, it would be obvious to a person of ordinary skill in the art to treat bipolar disorder with chelerythrine because it is taught in the art that chelerythrine is an antagonist of PKC and it is known in the art that lowering higher than normal PKC levels treats conditions such as bipolar disorder. One would be motivated to use chelerythrine, with a reasonable expectation of success, to treat bipolar disorder

because it is a PKC antagonist, of which it is known that PKC antagonists treat bipolar disorder.

Claims 12 and 14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Aylward et al. (PG-Pub 2003/0195168) in view of Herbert et al. (Biochemical and Biophysical Research Communications (1990) 172 (3), pgs. 993-999) as applied to claims 1-4, 10, 18 and 21 above and further in view of Goodman & Gilman's: The Pharmacological Basis of Therapeutics.

Goodman & Gilman's teaches routes of drug administration, including oral. It is taught that oral ingestion is the most common method of drug administration and the safest, most convenient and most economical (page 5).

Accordingly it would be obvious to employ oral drug administration as a route of administration of chelerythrine. One would be motivated because as is taught by Goodman & Gilman's, oral administration is one of the most common and safest routes of drug administration.

***Conclusion***

No claims are allowed.

***Contact Information***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Renee Claytor whose telephone number is 571-272-8394. The examiner can normally be reached on M-F 8:00-4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Renee Claytor

SREENI PADMANABHAN
SUPERVISORY PATENT EXAMINER